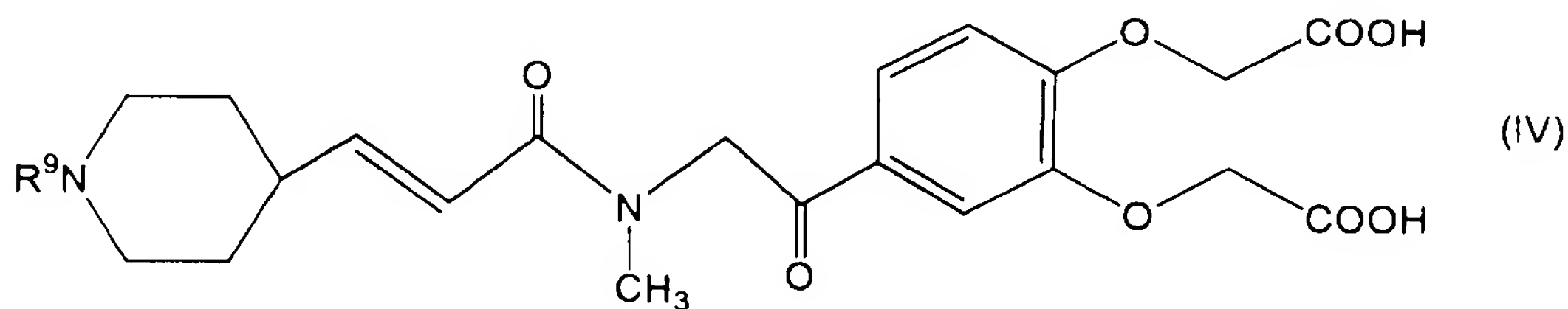


REMARKS

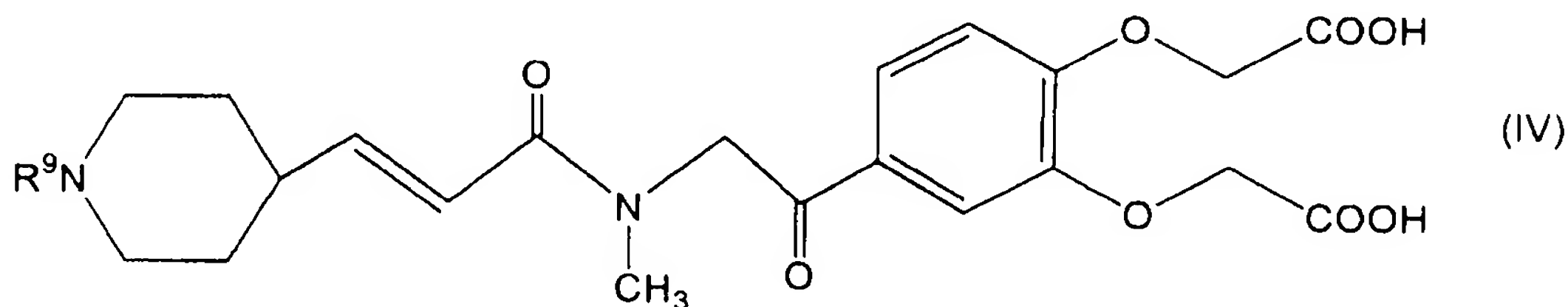
Claims 2, 5-7, and 9 are pending in the present application.

The presently claimed invention provides, *inter alia*, a compound represented by formula (IV):



wherein R⁹ represents a hydrogen atom or an amino protective group,
and a physiologically acceptable salt thereof. (see Claim 6)

The presently claimed invention further provides, *inter alia*, a contrast medium for thrombus that comprises, as an active substance, a substance obtained by labeling a compound capable of binding to glycoprotein IIb/IIIa selected from compounds represented by formula (IV):



wherein R⁹ represents a hydrogen atom or an amino protective group, wherein the compound capable of binding to glycoprotein IIb/IIIa is labeled with a positron emitting isotope;

and a physiologically acceptable salt thereof. (Claim 2)

Applicants submit that, for the reasons that follow, neither DeGrado et al, Katano et al, nor their combined disclosures render the claimed invention obvious.

The rejection of Claims 2, 5-7, and 9 under 35 U.S.C. §103(a) over DeGrado et al in view of Katano et al is respectfully traversed.

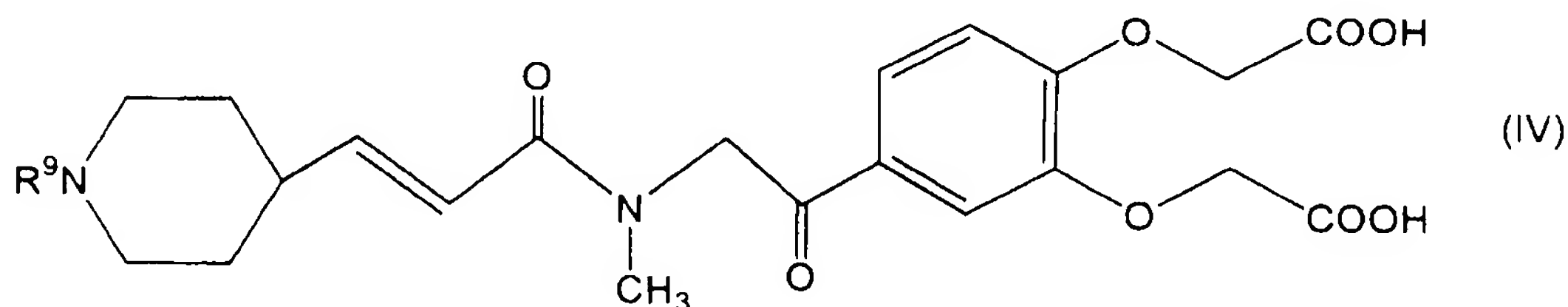
In the outstanding Office Action, the Examiner maintains that the claimed invention would be obvious in view of DeGrado et al in view of Katano et al. The Examiner's position is that Katano et al discloses a genus of compounds that embrace the compound of formula (IV) where R⁹ represents a hydrogen atom or an amino protective group. The Examiner further maintains that DeGrado et al discloses that radiolabeled cyclic compounds which act as antagonists of the platelet glycoprotein IIb/IIIa complex, including ¹¹C (a positron emitting isotope).

DeGrado et al do not disclose or suggest a "compound capable of binding to glycoprotein IIb/IIIa" in Claim 2 to compounds represented by formula (IV). The Examiner points to column 2 and column 3, lines 1-32 of Katano et al as disclosing the compound of formula (IV) in the claimed invention. Applicants submit that based on the overly broad disclosure at column 2 and column 3, lines 1-32 of Katano et al and the failure to exemplify any compounds within the scope of formula (IV) in the claimed invention (e.g., a compound where the "C₂₋₆ alkenylene at B is -CH=CH-), Katano et al fails to disclose a compound of formula (IV) in the claimed invention with sufficient specificity to permit the artisan to envisage this compound and/or to select this compound from the millions of possible alternatives.

Applicants submit that the Examiner has failed to support a proper *prima facie* case of obviousness. Specifically, as stated above, Katano et al disclose a genus that embraces millions of compounds, but does not provide any reasonable basis for the artisan to select a compound of formula (IV) from this overwhelming breadth. Further, Katano et al fails to

provide any reasonable expectation of success in using the compound as claimed. Moreover, DeGrado et al fails to provide any reasonable basis to select a positron emitting isotope or that the beneficial results obtained thereby would be achieved.

Further, in the disclosure of DeGrado et al the only exemplified radionuclides are ^{125}I , $^{99\text{m}}\text{Tc}$ and ^{111}In , which are not positron-emitting radionuclides and are detected using SPECT. Thus, at no point does DeGrado et al and/or Katano et al disclose or suggest a contrast medium for thrombus that comprises, as an active substance, a substance obtained by labeling a compound capable of binding to glycoprotein IIb/IIIa selected from compounds represented by formula (IV):



wherein R^9 represents a hydrogen atom or an amino protective group, wherein the compound capable of binding to glycoprotein IIb/IIIa is labeled with a positron emitting isotope; and a physiologically acceptable salt thereof. (Claim 2)

Even if the *prima facie* case of obviousness is proper, it can be rebutted by evidence of unexpected results for the claimed invention. To this end, we note that in the response filed August 3, 2010, Applicants argued:

Applicants submit that the importance of the labeling of the compound represented by formula (IV) labeled with a positron emitting isotope (e.g., ^{11}C) is clearly illustrated in the specification as filed. Specifically, in Examples 21 and 22 (pages 38-40 of the specification) Applicants have shown that the contrast mediums of Production Example 21 and 22 were accumulated in the thrombus with the ratio of approximately 24-fold and 4.8-fold (relative to blood) as well as approximately 95-fold and 16-fold (relative to muscle), respectively (see Table 2 on page 40 of the specification). Therefore, the contrast medium for thrombus of the present invention is demonstrated to specifically bind to the thrombus. This result is important in that with the present invention it is now “possible to carry

out the PET imaging of thrombus with low background noise and high resolution.” (page 40, lines 11-12 of the specification)

The Examiner dismisses this argument stating that “the compound of the combined disclosures encompasses the compound of the instant claims and is capable of the same functions and has the same properties.” This statement is without merit at least because the Examiner appears to be requiring that we compare the claimed invention with itself. However, “[a]lthough evidence of unexpected results must compare the claimed invention with the closest prior art, applicant is not required to compare the claimed invention with subject matter that does not exist in the prior art. *In re Geiger*, 815 F.2d 686, 689, 2 USPQ2d 1276, 1279 (Fed. Cir. 1987). Indeed, Applicants are not required to compare “the results of the invention with the results of the invention” see, *In re Chapman*, 357 F.2d 418, 422, 148 USPQ 711, 714 (CCPA 1966).

The Examiner also dismisses the foregoing evidentiary argument classifying it as “attorney argument”. This is simply untrue as the foregoing argument and the conclusions therein are taken from the specification at page 40. The specification was filed together with a Declaration by the inventors attesting to the truth and accuracy of all matters stated therein. Accordingly, the information contained in the specification carries the same weight as a “evidentiary” declaration filed during prosecution and in no way qualifies as “attorney argument”.

Moreover, Katano et al disclose conceptually the compounds of formula (IV), but do not disclose any specific compounds of this scope. In addition, Katano et al disclose that a group of compounds defined therein have an inhibitory activity of platelet aggregation, but do not disclose which compounds are suitable as a contrast media for thrombus with PET. In particular, Katano et al do not disclose or suggest that the compounds represented by formula

(IV) of the present invention have a superior effect as a contrast medium for thrombus with PET.

DeGrado et al disclose that a contrast medium for thrombus with PET can be obtained by labeling a GP IIb/IIIa related compound with a positron emitting radionuclide ^{11}C . However, all of the examples disclosed therein are directed to contrast media for SPECT labeled with gamma emitting radionuclide. No examples are provided of compounds labeled for PET.

As such, the skilled artisan would not envision based on the disclosures of DeGrado et al and Katano et al what type of structures of GP IIb/IIIa related compounds could be selected and how the compounds would be labeled with a positron emitting radionuclide in order to provide a contrast medium for thrombus with PET. Thus, based on the disclosures of DeGrado et al and Katano et al, the skilled artisan would not expect the superior contrast media for thrombus with PET can be obtained by selecting the compounds of formula (IV) of the present invention and labeling these compounds with a positron emitting radionuclide.

In order to label a compound with a gamma emitting radionuclide for SPECT (^{125}I , $^{99\text{m}}\text{Tc}$, etc.), it is necessary to introduce a radioelement that the original organic compound does not have. Accordingly, the labeled compound will have a chemical structure that is different from the original compound as a matter of course. Therefore, the skilled artisan would have no expectation of how the physiological activity intrinsic to the compound will change in the labeled compound. In contrast, the labeled compounds of the present invention maintain the physiological activity intrinsic to the original compound because the radionuclide is introduced by substituting, for example, one of the carbon atoms in the original compound with a positron emitting radionuclide. Accordingly, the chemical structures of the original compound is maintained.

A positron emitting radionuclide emits a positive electron from its atom and when the positive electron collides with a neighboring electron to be annihilated, emits a pair of annihilation radiations in directions opposite to each other by 180 degrees. In the case of PET, it is in principle possible that the two annihilation radiations are simultaneously photographed and the image obtained is analyzed with a computer and a very high-sensitivity image can be obtained.

This is in contrast to the gamma emitting radionuclide which emits one gamma ray (electromagnetic ray) from its atom. In the case of SPECT, the gamma ray is photographed and the image obtained is analyzed with a computer. Since the gamma ray has a lower energy than the annihilation radiations in PET, impacts within an organism such as absorption and scattering of the gamma ray is bigger. Therefore, SPECT is inferior in principle to PET in terms of resolution and quantitative measurement.

Thus, it is apparent that the contrast medium for PET is superior to the known contrast medium for SPECT in that PET allows achievement of a higher-sensitive image. However, the positron emitting radionuclide that is used for labeling has a very short half-life and accordingly is accompanied with a lot of restrictions to the labeling of a compound with the positron emitting radionuclide. Therefore, suitable compounds and reaction conditions can not be easily selected by the skilled artisan.

Even if diagnostic imaging agents for SPECT are known, it is not easy to prepare diagnostic imaging agents for PET by using a compound having the same mechanism. Therefore, only a limited number of products for diagnostic imaging for PET have been used.

With respect to the contrast media for thrombus, although contrast media for SPECT were disclosed in the cited references, contrast media for PET is not provided or known at the time of the present invention.

The present invention is the first case in which a positron emitting radionuclide, which is difficult to handle, was used to prepare a contrast medium for thrombus for PET and a high-resolution image of thrombus could be actually obtained. This is a result accomplished by selecting a GP IIb/IIIa related compound having a structure suitable for labeling with a positron emitting radionuclide and by establishing suitable conditions for labeling.

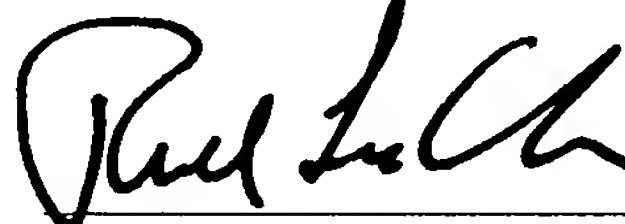
Applicants submit that DeGrado et al and Katano et al fail to provide the artisan with the claimed invention and that the claimed invention would not be obvious in view of these references.

Withdrawal of these grounds of rejection is requested.

Applicants respectfully submit that the above-identified application is now in condition for allowance, and early notice thereof is earnestly solicited.

Respectfully submitted,

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